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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Detailed Action
Election/Restriction

Please note that the instant application/case has been transferred to examiner Ganapathirama Raghu, Art Unit 1652, whose telephone number is (571)-272-4533 and all further enquiries regarding this application should be directed to said examiner.

Applicant's election with traverse of Group II, claims 2-6 for prosecution in their response dated 07/21/2008 is acknowledged. The traversal is on the grounds that the Groups I-III, claims 1-8 are linked as to form a single inventive concept under PCT Rule 13.1 as the cited prior art to break the unity of invention does not encode the polypeptide of the instant invention, although the prior art polypeptide and the polypeptide of the instant invention have similar activity, i.e., hydroxylase activity. Examiner has considered the applicants' request favorably to join Groups I-III encompassing claims 1-8. Claims 1-17 are pending in this application, claims 1-8 are now under consideration for examination. Claims 9-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/21/2008.

Priority

This application is a 371 of PCT/JP04/16297 filed on 11/04/2004 and claims the priority date of Japanese applications 2003-388165 filed on 11/18/2003 and 2004-165919 filed on 06/03/2004. Examiner notes that the English translations of said applications have not been provided. Applicants

have provided certified copies of Japanese applications 2003-388165 filed on 11/18/2003 and 2004-165919 filed on 06/03/2004, however no English translation of said applications have been provided. Furthermore, examiner is unable to find the elected sequence information in PCT/JP04/16297 filed on 11/04/2004. Therefore, the priority date for instant claims under consideration is deemed to be the filing date of the instant application filed on 05/15/2006.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 10/10/2007, 02/01/2007, 07/25/2006 and 05/15/2006 are in compliance with the provisions of 37 CFR 1.97. Accordingly, examiner has considered the information disclosure statements.

Claim Objections

Claims 1 part (d) and 2 part (d) recites the phrase "… a DNA hybridizable to a complementary DNA to said DNA under stringent conditions…", is grammatically awkward. Examiner suggests amending the claim to recite "…a DNA that hybridizes to the full complement of SEQ ID NO: 3 …". Appropriate correction is required.

Claims 3 and 4 as written is grammatically awkward; examiner suggests amending, i) claim 2 to recite "an isolated microorganism comprising the gene according to claim 2, wherein said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring." and ii) claim 3 to recite "an isolated microorganism comprising the gene according to claim 2 and other

carotenoid biosynthesis genes, wherein said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring."

Claim 8 is objected to, due to the following informality: Claim 8 has typographical/formatting error, lines 4-6 have gaps. Appropriate correction is required.

Claim Rejections: 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 2 are rejected under 35 U.S.C. 101, because the claim reads on non-statutory subject matter. Claims 1 and 2 are drawn to 'A peptide…', and 'A gene…' respectively which reads on the product of nature. Claims directed to such subject matter are considered non-statutory because they read on products of nature. Examiner suggests amending the claim to recite 'An isolated peptide …' and 'An isolated gene…' to show the hand of man, in order to overcome the rejection.

Claim Rejections 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 and claims 3-8 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 part (d) and 2 part (d) recites the phrase "a bacterium-derived

peptide". It is not clear to the examiner as to what the phrase "a bacterium-derived peptide…" means in the context of the above claims, is this synonymous with "obtained from specific strain of bacterium" or does it include natural and man-made mutants thereof from any source. Furthermore, literally while the term "derived" means to "to isolate from or obtain from a source", the above term could also mean "to arrive by reasoning i. e., to deduce or infer" or also mean "to produce from another substance". It is noted that while the term "derived" will encompass proteins naturally found in a bacterium, the term in its broadest reasonable interpretation will also encompass any variant artificially created of a bacterial β-ionone ring-2-hydroxylase. Since a protein activity is defined by its structure, if a man-made variant of a bacterial β-ionone ring-2-hydroxylase enzyme has the same structure (i. e., amino acid sequence) as that of a protein isolated from an organism which is not a β-ionone ring-2-hydroxylase enzyme, the term "derived…" would not allow one of skill in the art to differentiate between these proteins. Therefore, unless applicant has defined the term "derived…" as equivalent to "obtained from specific strain of bacteria", the term "derived…" does not further limit the recited enzyme. Clarification and correction is required.

Claims 1 and 2 and claims 3-8 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 part (d) and 2 part (d) recites the phrase "… a DNA hybridizable to a complementary DNA to said DNA under stringent conditions…",

but does not recite conditions under which the hybridization must occur. Nucleic acids which hybridize under one set of conditions may not hybridize under other conditions and it is well known in the art that stringent conditions can be described as high stringency, medium stringency or low stringency. It is not clear to the examiner as to what type of stringency is encompassed in the above phrase. Thus the scope of the claims is unclear. A perusal of the specification, on page 15, first paragraph describes exemplary hybridization conditions, however claims as written do not recite the specific conditions the applicants' intend to encompass. Clarification and correction is required.

Claim Rejections: 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1 and 2 and claims 3-8 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, because the specification is being enabling for an isolated polypeptide of SEQ ID NO: 4 having β-ionone ring-2-hydroxylase activity and encoded by a polynucleotide sequence of SEQ ID NO: 3, isolated microorganism comprising said polynucleotide and encoding said polypeptide and to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8), does not reasonably provide enablement for: i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the

amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 3); iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 4); iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate (as in claims 5 and 6); and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of

working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-8 are so broad as to encompass: i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 3); iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 4); iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate (as in claims 5 and 6); and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8). The scope of the claims are not

commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides and encoding nucleotide sequences i.e., i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 4); and iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate (as in claims 5 and 6), broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are

tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to making and the use of an isolated polypeptide of SEQ ID NO: 4 having β-ionone ring-2-hydroxylase activity and encoded by a polynucleotide sequence of SEQ ID NO: 3, isolated microorganism comprising said polynucleotide and encoding said polypeptide and to a method for preparing hydroxylated carotenoids by culturing said microorganism, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed peptides and encoding nucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the peptides and encoding nucleotides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications as required by the instant claims. The specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable (e.g., see Whisstock et al., Q Rev Biophys. 2003

Aug; 36(3): 307-340). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish even further with additional modification, e.g. multiple substitutions or deletions or insertions or transpositions.

The specification does not support the broad scope of the claims i.e., i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3; ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring; iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring; iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate; and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism, as claimed in claims

1-8, because the specification does not establish: (A) regions of the peptide/nucleotide structure which may be modified without affecting the activity of β-ionone ring-2-hydroxylase activity; (B) the general tolerance of the peptide and the nucleotide encoding the activity of β-ionone ring-2-hydroxylase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue or the respective codon in the nucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including peptides and encoding nucleotide sequence with an enormous number of modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of peptides and encoding nucleotides i.e., i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3; ii) a microorganism comprising said gene and said microorganism

is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring; iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring; iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate; and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism, broadly encompassed by the claims is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8 are directed to encompass: i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4

and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 3); iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 4); iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate (as in claims 5 and 6); and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8).

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative

number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Claims 1-8 are rejected under this section 35 U.S.C. 112, because the claims as interpreted, are directed to encompass a genus of polypeptides and encoding polynucleotides i. e., i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 3); iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 4); iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from

farnesyl pyrophosphate (as in claims 5 and 6); and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8).

No description of identifying characteristics of all of the sequences of : i) peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3; ii) any other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring; and iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate, has been provided by the applicants in the specification.

No information, beyond the characterization of an isolated polypeptide of SEQ ID NO: 4 having β-ionone ring-2-hydroxylase activity and encoded by a polynucleotide sequence of SEQ ID NO: 3, isolated microorganism comprising said polynucleotide and encoding said polypeptide and to a method for preparing hydroxylated carotenoids by culturing said microorganism has been provided by

the applicants, which would indicate that they had possession of the claimed genus of the polypeptides and encoding polynucleotides i.e., i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 3); iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 4); iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate (as in claims 5 and 6); and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8).

In the instant case, there is no structure associated with functional limitations recited with regard to the members of the genus of polypeptides and

encoding polynucleotides, and the specification fails to provide any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 or ii) any other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring; and iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate.

Furthermore; i) neither the prior art at the time of filing of the instant application nor the specification provides information regarding catalytic domains, the binding domains, the core motifs and 3D model or the defined core regions/motifs involved in the desired biological activity/enzymological characteristics of the polypeptide i.e., β-ionone ring-2-hydroxylase activity, the tertiary structure of the molecule and folding patterns that are essential for the desired biological activity/enzymological characteristics. Therefore, examiner takes the position that due to the paucity of information regarding structure-

function correlation, the specification lacks identifying characteristics of all of the sequences especially of any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3, within the claimed genus.

The genus of polynucleotides and encoded polypeptides required in the claimed invention is an extremely large structurally and functionally variable genus. While the argument can be made that the recited genus of polypeptides and encoding polynucleotides is adequately described by the disclosure of the structure of an isolated polypeptide of SEQ ID NO: 4 having β-ionone ring-2-hydroxylase activity and encoding polynucleotide of SEQ ID NO: 3, since one could use structural homology to isolate those polynucleotides and encoded polypeptides recited in the claims. As taught by the art, even highly structurally homologous polynucleotides and encoded polypeptides do not necessarily share the same function i.e., conservation of structure is not necessarily a surrogate for conservation of function. For example, Witkowski et al., (Biochemistry 38:11643-11650, 1999), teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al., (J. Bacteriol., 183(8): 2405-2410, 2001), teaches that two naturally occurring *Pseudomonas* enzymes having 98%

amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al., (Science 282:1315-1317, 1998), teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Therefore, the claimed genera of polypeptides and encoding polynucleotides include widely variable structure and associated functions, since minor changes in structure may result in changes affecting function and no additional information correlating structure with distinct enzymological characteristics has been provided.

Due to the fact that the specification only discloses an isolated polypeptide of SEQ ID NO: 4 having β-ionone ring-2-hydroxylase activity and encoded by a polynucleotide sequence of SEQ ID NO: 3, isolated microorganism comprising said polynucleotide and encoding said polypeptide and to a method for preparing hydroxylated carotenoids by culturing said microorganism, and the lack of description of any additional species/variants/mutants/recombinants by any relevant, identifying characteristics or properties or structure-function correlationship for the recited β-ionone ring-2-hydroxylase, one of skill in the art would not recognize from the disclosure that applicant was in possession of the claimed invention.

Applicants are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Nishida et al., (Appl. Environ. Microbiol., 2005, Vol. 71 (8): 4286-4296 in IDS). Note, examiner is unable to find the elected sequence information in PCT/JP04/16297 filed on 11/04/2004, therefore, the priority date for instant claims under consideration is deemed to be the filing date of the instant application filed on 05/15/2006.

Claims 1-8 are directed to: i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 3); iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group

at the position 2 carbon of β-ionone ring (as in claim 4); iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate (as in claims 5 and 6); and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8).

Nishida et al., (*supra*) specifically teach isolated polypeptide having β-ionone ring-2-hydroxylase activity and the encoding polynucleotide, said reference polypeptide and encoding polynucleotide having 100% sequence homology to SEQ ID NO: 4 and encoding polynucleotide sequence SEQ ID NO: 3 of the instant application. Said reference also teaches isolated microorganism comprising said polynucleotide and encoding said polypeptide and to a method for preparing hydroxylated carotenoids by culturing said microorganism (Abstract and entire document). Therefore, the reference of Nishida et al., (Appl. Environ. Microbiol., 2005, Vol. 71 (8): 4286-4296 in IDS) anticipates claims 1-8 of the present invention.

Claims 1-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Tao et al., (Gene, 2006, Vol. 379; 101-108, available online 05/03/2006). Note, examiner is unable to find the elected sequence information in PCT/JP04/16297 filed on 11/04/2004, therefore, the priority date for instant claims under

consideration is deemed to be the filing date of the instant application filed on 05/15/2006.

Claims 1-8 are directed to: i) any peptide comprising an amino acid sequence of SEQ ID NO: 4, wherein one or several amino acid residues are added, deleted, substituted or a peptide consisting of an amino acid sequence having a 50% or more identity with the amino acid sequence of SEQ ID NO: 4 and having β-ionone ring-2-hydroxylase activity and said peptide encoded by a gene having a nucleotide sequence that hybridizes under any undefined stringent conditions to a nucleotide sequence shown in SEQ ID NO: 3 (as in claims 1 and 2); ii) a microorganism comprising said gene and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 3); iii) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants and said microorganism is capable of introducing a hydroxyl group at the position 2 carbon of β-ionone ring (as in claim 4); iv) a microorganism comprising said gene and other carotenoid biosynthesis genes from any source including variants, mutants and recombinants, wherein said other carotenoid biosynthesis genes are all or any part of a gene cluster from any source including variants, mutants and recombinants required for synthesizing β-ionone ring containing carotenoids from farnesyl pyrophosphate (as in claims 5 and 6); and v) to a method for preparing hydroxylated carotenoids by culturing said microorganism (as in claims 6-8).

Tao et al., (*supra*) specifically teach isolated polypeptide having β-ionone ring-2-hydroxylase activity and the encoding polynucleotide, said reference polypeptide having 98.8% sequence homology to of SEQ ID NO: 4 of the instant application. Said reference also teaches isolated microorganism comprising said polynucleotide and encoding said polypeptide and to a method for preparing hydroxylated carotenoids by culturing said microorganism (Abstract and entire document). Therefore, the reference of Tao et al., (Gene, 2006, Vol. 379; 101-108, available online 05/03/2006) anticipates claims 1-8 of the present invention.

Allowable Subject Matter/Conclusion

None of the claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

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